AMENDMENTS TO THE CLAIMS

WHAT IS CLAIMED IS:

Claim 1. (Currently Amended) A method of modulating calvarial osteoblast differentiation and mineralization in a human being, said method comprising:

altering expression or activity of Nell-1, in the human being, wherein increased expression or activity of Nell-1 increases osteoblast differentiation or mineralization and decreased expression or activity of Nell-1 decreases osteoblast differentiation or mineralization in the human being.

Claim 2. (Currently Amended) The method of claim 1, wherein Nell-1 expression or activity is inhibited ~~is~~ by a method selected from the group consisting of an anti-Nell-1 antisense molecule, a Nell-1 specific riibozyme, a Nell-1 specific catalytic DNA, a Nell-1 specific RNAi, anti-Nell-1 intrabodies, and gene therapy approaches that knock out Nell-1 in ~~particular~~ target cells and/or tissues.

Claim 3. (Original) The method of claim 1, wherein Nell-1 expression or activity is increased by a method selected from the group consisting of transfecting a cell with an exogenous nucleic acid expressing Nell-1, and transfecting a cell with a Nell-1 protein.

Claim 4. (Currently Amended) The method of claim 2, wherein said Nell-1 expression or activity is inhibited in ~~a mammal~~ the human, and

wherein the human being is experiencing abnormal cranial suture development.

Claim 5. (Currently Amended) The method of claim 4, wherein said abnormal cranial suture development comprises ~~Craniosynostosis~~ craniosynostosis (CS).

Claim 6. (Currently Amended) A method of facilitating latent TGF-~~β~~β1 activation in a ~~mammal~~ human being, said method comprising administering exogenous Nell-1 to said ~~mammal~~ human being, or increasing expression activity of endogenous Nell-1 in ~~said mammal~~ the human being.

Claim 7. (Currently Amended) A method of activating or sequestering a member of the TGF-~~ß~~β superfamily in a ~~mammal~~ human being, said method comprising administering exogenous Nell-1 to said ~~mammal~~ human being, or increasing expression activity of endogenous Nell-1 in ~~said mammal~~ the human being.

Claim 8. (Currently Amended) A method of screening for an agent that modulates osteoblast differentiation, said method comprising:

contacting a test cell which is a human cell containing a ~~*NELL*~~ Nell-1 gene with a test agent; and

detecting a change in the expression level of a ~~*NELL*~~ Nell-1 gene or the activity of Nell-1 in said test cell as compared to the expression of the ~~*NELL*~~ Nell-1 gene or the activity of Nell-1 in a control cell where a difference in the expression level of ~~*NELL*~~ Nell-1 or the activity of Nell-1 in the test cell and the control cell indicates that said agent modulates bone mineralization.

Claim 9. (Original) The method of claim 8, wherein said control is a negative control cell contacted with said test agent at a lower concentration than said test cell.

Claim 10. (Original) The method of claim 9, wherein said lower concentration is the absence of said test agent.

Claim 11. (Original) The method of claim 8, wherein said control is a positive control cell contacted with said test agent at a higher concentration than said test cell.

Claim 12. (Currently Amended) The method of claim 8, further comprising recording test agents that alter expression of the ~~*NELL*~~ Nell-1 nucleic acid or the ~~*NELL*~~ Nell-1 protein in a database of modulators of ~~*NELL*~~ Nell-1 activity or in a database of modulators of bone mineralization.

Claim 13. (Currently Amended) The method of claim 8, wherein the expression level of ~~nell~~ Nell-1 is detected by measuring the level of ~~*NELL*~~ Nell-1 mRNA in said cell.

Claim 14. (Currently Amended) The method of claim 13, wherein said level of ~~*NELL*~~ Nell-1 mRNA is measured by hybridizing said mRNA to a probe that specifically hybridizes to a ~~*NELL*~~ Nell-1 nucleic acid.

Claim 15. (Currently Amended) The method of claim 14, wherein said hybridizing is according to a method selected from the group consisting of a Northern blot, a Southern blot using DNA derived from the ~~nell~~ Nell-1 RNA, an array hybridization, an affinity chromatography, and an *in situ* hybridization.

Claim 16. (Original) The method of claim 15, wherein said probe is a member of a plurality of probes that forms an array of probes.

Claim 17. (Currently Amended) The method of claim 13, wherein said level of ~~*NELL*~~ Nell-1 mRNA is measured using a nucleic acid amplification reaction.

Claim 18. (Currently Amended) The method of claim 8, wherein said level of ~~*NELL*~~ Nell-1 is detected by determining the expression level of a ~~*NELL*~~ Nell-1 protein in said biological sample.

Claim 19. (Original) The method of claim 18, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

Claim 20. (Original) The method of claim 8, wherein said cell is cultured *ex vivo*.

Claim 21. (Original) The method of claim 8, wherein said test agent is not an antibody.

Claim 22. (Original) The method of claim 8, wherein said test agent is not a protein.

Claim 23. (Currently Amended) A method of altering Nell-1 expression in a ~~mammalian~~ human cell, said method comprising altering the expression or activity of *Msx2* and/or ~~*Cbfa1*~~ *Cafa1* in the human cell.

Claim 24. (Currently Amended) The method of claim 23, comprising upregulating *Cbfa1* expression or activity in the human cell to upregulate Nell-1 expression or activity.

Claim 25. (Currently Amended) The method of claim 23, comprising upregulating Msx2 expression or activity in the human cell to downregulate Nell-1 expression or activity.

Claim 26. (Currently Amended) A method of screening for an agent that modulates Nell-1 expression or activity in a human being, said method comprising:

contacting a test cell which is a human cell containing a *Cbfa1* and/or an *Msx2* gene with a ~~20~~ test agent; and

detecting a change in the expression level of an *Cbfa1* ~~and/or an Msx2gene or the activity of *Cbfa1* and/or an Msx2 in said test cell as compared to the expression of the *Cbfa1*~~ and/or an *Msx2* gene or the activity of Cbfa1 and/or an Msx2 in said test cell as compared to the expression of the *Cbfa1* and/or an *Msx2* gene or the activity of Cbfa1 and/or an Msx2 in a control cell where a difference in the expression level of *Cbfa1* and/or an *Msx2* or the activity of Cbfa1 and/or an Msx2 in the test cell and the control cell indicates that said agent modulates Nell-1 expression or activity.

Claim 27. (Original) The method of claim 26, wherein said control is a negative control cell contacted with said test agent at a lower concentration than said test cell.

Claim 28. (Original) The method of claim 27, wherein said lower concentration is the absence of said test agent.

Claim 29. (Original) The method of claim 26, wherein said control is a positive control cell contacted with said test agent at a higher concentration than said test cell.

Claim 30. (Currently Amended) The method of claim 26, further comprising recording test agents that alter expression of *Cbfa1* ~~and/or an Msx2 gene or the activity of Cbfa1~~ and/or an *Msx2* gene or the activity of Cbfa1 and/or an Msx2 in a database of modulators of ~~*NELL*~~ Nell-1 activity or in a database of modulators of bone mineralization.

Claim 31. (Currently Amended) The method of claim 26, wherein the expression level of ~~nell~~ Nell-1 is detected by measuring the level of *Cbfa1* and/or an *Msx2* mRNA in said cell.

Claim 32. (Currently Amended) The method of claim 31, wherein said level of *Cbfa1* and/or an *Msx2* mRNA is measured by hybridizing said mRNA to a probe that specifically hybridizes to a ~~15~~ *Cbfa1* and/or an *Msx2* nucleic acid.

Claim 33. (Original) The method of claim 32, wherein said hybridizing is according to a method selected from the group consisting of a Northern blot, a Southern blot using DNA derived from the *Cbfa1* and/or *Msx2* RNA, an array hybridization, an affinity chromatography, and an *in situ* hybridization.

Claim 34. (Original) The method of claim 33, wherein said probe is a member of a plurality of probes that forms an array of probes.

Claim 35. (Currently Amended) The method of claim 31, wherein said level of *Cbfa1* and/or *Msx2* ~~mRNA~~ RNA is measured using a nucleic acid amplification reaction.

Claim 36. (Original) The method of claim 26, wherein said level of *Cbfa1* and/or *Msx2* is detected by determining the expression level of a *Cbfa1* and/or *Msx2* protein in said biological sample.

Claim 37. (Original) The method of claim 36, wherein said detecting is via a method selected from the group consisting of capillary electrophoresis, a Western blot, mass spectroscopy, ELISA, immunochromatography, and immunohistochemistry.

Claim 38. (Original) The method of claim 26, wherein said cell is cultured *ex vivo*.

Claim 39. (Original) The method of claim 26, wherein said test agent is not an antibody.

Claim 40. (Original) The method of claim 26, wherein said test agent is not a protein.

Claim 41. (Currently Amended) A pharmaceutical formulation~~, said formulation~~ comprising:

one or more active agents in an amount effective for increasing osteoblast differentiation or mineralization in a human being selected from the group consisting of a nucleic acid encoding a Nell-1 protein, a Nell-1 protein, and an agent that alters expression ~~10~~ or activity of a Nell-1 protein; and

a pharmaceutically acceptable excipient.